App No.: Not Yet Assigned Docket Not Inventors: Hassan PAJOUHESH et al.

Title: N-TYPE CALCIUM CHANNEL BLOCKERS Docket No.: 381092001600

P A T E N T Docket <u>381092001600</u>

No.	Compound	Name
P1	Meo X	(R)-N-{1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-pyrrolidin-3-yl}-3,5-di-tert-butyl-4-methoxy-N-methyl-benzamide
P2	Meo Solo Solo Solo Solo Solo Solo Solo So	(R)-6,6-Bis-(4-fluoro-phenyl)-hexanoic acid [1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-pyrrolidin-3-yl]-methyl-amide
P3		(R)-N-(1-Benzhydryl-pyrrolidin-3-yl)-N- methyl-3,3-diphenyl-propionamide
P4	F OMe	(S)-N-{1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-pyrrolidin-3-yl}-3,5-di-tert-butyl-4-methoxy-N-methyl-benzamide
P5	Meo Y O	(S)-6,6-Bis-(4-fluoro-phenyl)-hexanoic acid [1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-pyrrolidin-3-yl]-methyl-amide
P6		(S)-N-(1-Benzhydryl-pyrrolidin-3-yl)-N- methyl-3,3-diphenyl-propionamide
P7		(R)-N-Methyl-3,3-diphenyl-N-(1-pyridin-4-ylmethyl-pyrrolidin-3-yl)-propionamide
P8		(R)-N-Methyl-3,3-diphenyl-N-(1-pyridin-3-ylmethyl-pyrrolidin-3-yl)-propionamide

Figure 1

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No.	Compound	Name
P9		(R)-N-Methyl-3,3-diphenyl-N-(1-pyridin-2-ylmethyl-pyrrolidin-3-yl)-propionamide
P10		(R)-N-Methyl-3,3-diphenyl-N-[1-(phenyl-pyridin-4-yl-methyl)-pyrrolidin-3-yl]- propionamide
P11		(R)-N-Methyl-3,3-diphenyl-N-[1-(phenyl-pyridin-3-yl-methyl)-pyrrolidin-3-yl}- propionamide
P12		(R)-N-Methyl-3,3-diphenyl-N-[1-(phenyl-pyridin-2-yl-methyl)-pyrrolidin-3-yl]- propionamide
P13		(S)-N-Methyl-3,3-diphenyl-N-(1-pyridin-4-ylmethyl-pyrrolidin-3-yl)-propionamide
P14		(S)-N-(1-Benzhydryl-pyrrolidin-3-yl)-2- diphenylamino-N-methyl-acetamide
P15		(S)-2-[(1-Benzhydryl-pyrrolidin-3-yl)-methyl-amino]-N,N-diphenyl-acetamide
P16		(S)-3-Benzhydryl-1-(1-benzhydryl- pyrrolidin-3-yl)-1-methyl-urea

Figure 1

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No.	Compound	Name
P17		(S)-N-Methyl-3,3-diphenyl-N-(1-pyridin-3-ylmethyl-pyrrolidin-3-yl)-propionamide
P18		(S)-N-Methyl-3,3-diphenyl-N-(1-pyridin-2-ylmethyl-pyrrolidin-3-yl)-propionamide
P19	F OME	(R)-{1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]- pyrrolidin-3-yl}-(3,5-di-tert-butyl-4- methoxy-benzyl)-methyl-amine
P20	Meo F	(R)-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-[1- (3,5-di-tert-butyl-4-methoxy-benzyl)- pyrrolidin-3-yl]-methyl-amine
P21	F CMe	(S)-{1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]- pyrrolidin-3-yl}-(3,5-di-tert-butyl-4- methoxy-benzyl)-methyl-amine
P22	Meo F	(S)-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-[1- (3,5-di-tert-butyl-4-methoxy-benzyl)- pyrrolidin-3-yl]-methyl-amine
P23	CI ON NEO	(R)-N-{1-[(4-Chloro-phenyl)-phenyl-methyl]-pyrrolidin-3-yl}-N-methyl-3,3-diphenyl-propionamide
P24		(S)-N-{1-[(4-Chloro-phenyl)-phenyl-methyl]-pyrrolidin-3-yl}-N-methyl-3,3-diphenyl-propionamide

Figure 1

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No.	Compound	Name
P25	CI NY NY O	(R)-N-{1-[(3-Chloro-phenyl)-phenyl- methyl]-pyrrolidin-3-yl}-N-methyl-3,3- diphenyl-propionamide
P26		(S)-N-{1-[(3-Chloro-phenyl)-phenyl-methyl]-pyrrolidin-3-yl}-N-methyl-3,3-diphenyl-propionamide
P27		(R)-N-{1-[(2-Chloro-phenyl)-phenyl-methyl]-pyrrolidin-3-yl}-N-methyl-3,3-diphenyl-propionamide
P28	CI NI	(S)-N-{1-[(2-Chloro-phenyl)-phenyl-methyl]-pyrrolidin-3-yl}-N-methyl-3,3-diphenyl-propionamide
P29		(R)-N-{1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-pyrrolidin-3-yl}-3,5-di-tert-butyl-N-methyl-benzamide
P30		(R)-6,6-Bis-(4-fluoro-phenyl)-hexanoic acid [1-(3,5-di-tert-butyl-benzoyl)-pyrrolidin-3- yl]-methyl-amide
P31		(S)-N-{1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-pyrrolidin-3-yl}-3,5-di-tert-butyl-N-methyl-benzamide

Figure 1

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No.	Compound	Name
P32		(S)-6,6-Bis-(4-fluoro-phenyl)-hexanoic acid [1-(3,5-di-tert-butyl-benzoyl)-pyrrolidin-3-yl]-methyl-amide
P33		(R)-N-{1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-pyrrolidin-3-yl}-4-tert-butyl-N-methyl-benzamide
P34		(R)-6,6-Bis-(4-fluoro-phenyl)-hexanoic acid [1-(4-tert-butyl-benzoyl)-pyrrolidin-3-yl]-methyl-amide
P35		(S)-N-{1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-pyrrolidin-3-yl}-4-tert-butyl-N-methyl-benzamide
P36		(S)-6,6-Bis-(4-fluoro-phenyl)-hexanoic acid [1-(4-tert-butyl-benzoyl)-pyrrolidin-3-yl]-methyl-amide
P37		(S)-N-Methyl-N-[1-(1-methyl-piperidin-4-ylmethyl)-pyrrolidin-3-yl]-3,3-diphenyl-propionamide
P38		(S)-N-Methyl-N-[1-(1-methyl-piperidin-3-ylmethyl)-pyrrolidin-3-yl]-3,3-diphenyl-propionamide
P39		(S)-N-Methyl-N-[1-(1-methyl-piperidin-2-ylmethyl)-pyrrolidin-3-yl]-3,3-diphenyl-propionamide

Figure 1

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No.	Compound	Name
P40		4-[6,6-Bis-(4-fluoro-phenyl)- hexanoylamino]-1-(3,5-di-tert-butyl-4- methoxy-benzoyl)-pyrrolidine-2-carboxylic acid ethyl ester
P41		4-[6,6-Bis-(4-fluoro-phenyl)- hexanoylamino]-1-(3,5-di-tert-butyl-4- methoxy-benzoyl)-pyrrolidine-2-carboxylic acid
P42		1-Benzhydryl-4-(3,3-diphenyl- propionylamino)-pyrrolidine-2-carboxylic acid ethyl ester
P43		1-Benzhydryl-4-(3,3-diphenyl- propionylamino)-pyrrolidine-2-carboxylic acid
P44		N-(1-Benzhydryl-2-oxo-pyrrolidin-3-yl)- 3,3-diphenyl-propionamide
P45		1-Benzhydryl-3-(1-benzhydryl-2-oxo- pyrrolidin-3-yl)-urea
P46		N-(1-Benzhydryl-2-oxo-pyrrolidin-3-yl)-2- diphenylamino-acetamide
P47		2-(1-Benzhydryl-2-oxo-pyrrolidin-3- ylamino)-N, N-diphenyl-acetamide

Figure 1

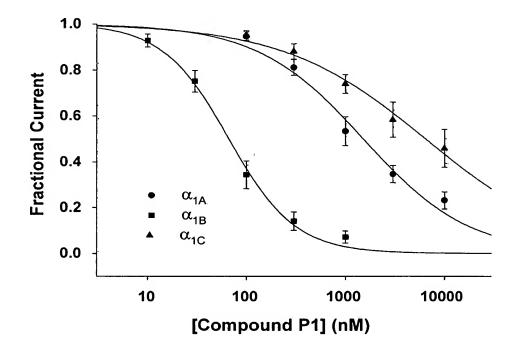
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P A T E N T Docket 381092001600

Effect of Compound P1 on Various HVA Ca2+ Channels



P/Q-type $IC_{50} = 1722 \pm 429 \text{ nM (n=5)}$

N-type $IC_{50} = 74 \pm 17 \text{ nM} \text{ (n=5)}$

L-type $IC_{50} = 5617 \pm 1706 (n=4)$

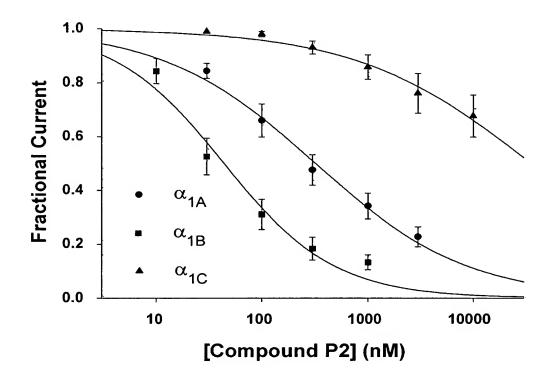
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Inventors: Hassan PAJOUHESH et al.

Title: N-TYPE CALCIUM CHANNEL BLOCKERS

P A T E N T Docket 381092001600

Effect of Compound P2 on Various HVA Ca2+ Channels



P/Q-type $IC_{50} = 428 \pm 140 \text{ nM} \text{ (n=6)}$

N-type $IC_{50} = 46 \pm 6 \text{ nM (n=5)}$

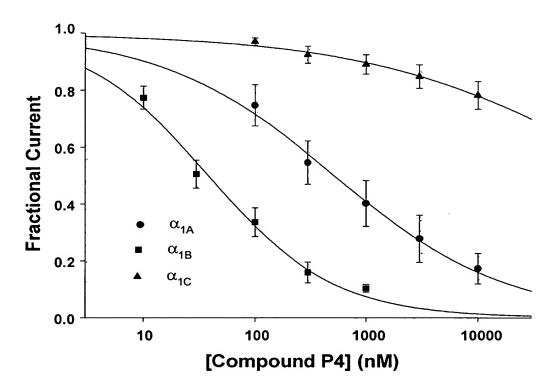
L-type IC₅₀ >>10 μ M (n=5) (estimate :66 μ M)

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Title: N-TYPE CALCIUM CHANNEL BLOCKERS

P A T E N T Docket 381092001600

Effect of Compound P4 on Various HVA Ca2+ Channels



P/Q-type $IC_{50} = 518 \pm 47 \text{ nM} \text{ (n=6)}$

N-type $IC_{50} = 43 \pm 12 \text{ nM (n=5)}$

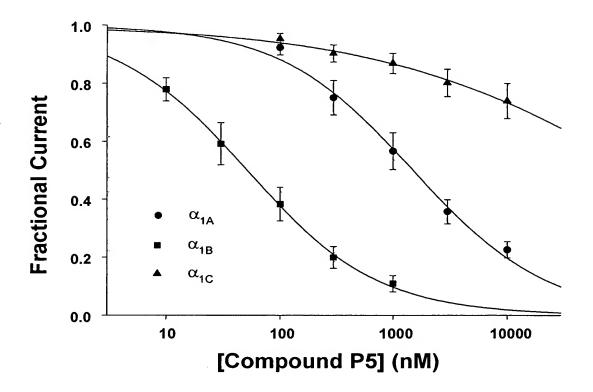
L-type IC₅₀ >>10 μ M (n=5) (estimate : 230 μ M)

Inventors: Hassan PAJOUHESH et al.

Title: N-TYPE CALCIUM CHANNEL BLOCKERS

P A T E N T Docket 381092001600

Effect of Compound P5 on Various HVA Ca2+ Channels



P/Q-type $IC_{50} = 1721 \pm 473 \text{ nM (n=5)}$

N-type $IC_{50} = 56 \pm 12 \text{ nM (n=5)}$

L-type IC₅₀ >>10 μ M (n=5) (estimate :146 μ M)